AD			

Award Number: DAMD17-99-2-9025

TITLE: The Associate Program in Ethnobiology, Socio-Economic Value Assessment and Community Based Conservation

PRINCIPAL INVESTIGATOR: Maurice M. Iwu, Ph.D.

CONTRACTING ORGANIZATION: Bioresources Development and
Conservation Programme
Silver Spring, Maryland 20902

**REPORT DATE: October 1999** 

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

## REPORT DOCUMENTATION PAGE

Form Approved OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project Cardon 1828. Washington Project Cardon 1829 Washi

(0704-0188), Washington, DC 20503					
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE October 1999		REPORT TYPE AND DATES COVERED		
4. TITLE AND SUBTITLE The Associate Program in Ethnobiology Based Conservation		Annual (1-Oct-98 - 30-Sep-99)  ssment and Community  5. FUNDING NUMBERS DAMD17-99-2-9025			
6. AUTHOR(S) Maurice M. Iwu, Ph.D.			-		
7. PERFORMING ORGANIZATION NA Bioresources Development and Cor Silver Spring, Maryland 20902			8. PERFORMIN REPORT NU	G ORGANIZATION MBER	
E-MAIL: iwum@bioresources.org					
9. SPONSORING / MONITORING AGE	NCY NAME(S) AND ADDRESS(E	(S)		NG / MONITORING EPORT NUMBER	
U.S. Army Medical Research and M Fort Detrick, Maryland 21702-5012					
11. SUPPLEMENTARY NOTES					
12a. DISTRIBUTION / AVAILABILITY Approved for public release; distrib				12b. DISTRIBUTION CODE	
13. ABSTRACT (Maximum 200 Words) leading to the isolation of tantimalarial candidate. They chlorantha, Spathodea came Glossocalyx brevipes, Cleis	pioactive compounds. They include: Picralima na papanulata, Synclisia sc papanolis patens, Leido	he following plan itida, Araliopsis arbrida, Uvaria botrys staudtii a	its are in our tabouensis, M chamae, Cry nd Pachypoda	priority list as potentia Morinda lucida, Enantia Syptolepis sanguinolenta Anthium staudtii. Thre	

13. ABSTRACT (Maximum 200 Words) BDCP conducted extraction and bioassay guided fractionation of active extract leading to the isolation of bioactive compounds. The following plants are in our priority list as potentia antimalarial candidate. They include: Picralima nitida, Araliopsis tabouensis, Morinda lucida, Enantic chlorantha, Spathodea campanulata, Synclisia scarbrida, Uvaria chamae, Cryptolepis sanguinolenta Glossocalyx brevipes, Cleistopholis patens, Leidobotrys staudtii and Pachypodanthium staudtii. Three compounds derived from a modification of the parent cryptolepine molecule which showed very significan antimalarial have been synthesized to enable in vivo testing. Six compounds identified from earlier studies are being evaluated against four strains of Trypanosoma b.brucei and three T.b.rhodesiense clinical isolates. Fou new plants namely Plantex vellous, Glossocalyx brevipes, Fagara lemairei, Dorsternia bateri showed very promising result. Three cryptolepine analogs found to possessing broad-spectrum antiprotozoal activity will be screened in vivo against Cryptosporidium and Toxoplasmosis. Results from the non-specific brine-shrimg studies have been compared with those obtained from our anti-malarial screens. There seems to be a correlation between brine-shrimp toxicity and antimalarial activity. Additional data are being collected to validate this relationship. Significant efforts in database integration into CISAMAP, phytomedicine, socio-economic valuation studies, training and trust fund development were made this year.

14. SUBJECT TERMS			15. NUMBER OF PAGES
anti-malaria, plant collection,	19		
Fractionation, phytomedicine, database, trust fund, socio-economic evaluation.			16. PRICE CODE
17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	OF THIS PAGE Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89) Prescribed by ANSI Std. Z39-18 298-102

## **FOREWORD**

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.
X_ Where copyrighted material is quoted, permission has been obtained to use such material.
X_ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.
_X_ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.
N/A In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).
N/A For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.
N/A In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.
N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.
N/A In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.
PI - Signature Date

## **TABLE OF CONTENTS:**

Report Docur	mentatio	n Page.			••	••	••		••		2
Foreword	••	••		••		••					3
Introduction	••					••		••	••		5
Body	••				••	••	••	••			6
Drug ?	Develop	ment					••		••		6
Antim	alarial a	activity.		••				••			6
Antile	ishmani	asis and	d Antitr	ypanoso	omiasis.		.,		••		6
Tricho	omonas.			••	••						7
Antiv	iral Acti	vity			••			••			7
Oppor	rtunistic	Infection	ons								7
C.N.S	. Activi	ty									7
Phyto	medicin	e Devel	opment								7
Information N	<b>Manage</b> r	nent									8
Socio-Econor	nic Valı	ie Asse	ssment :	Studies.	•••		••				8
Overv	iew							••			8
Metho	odology	and nat	ure of d	ata							9
Result	ts and D	iscussic	ons								9
Implic	cations										13
Capacity and	Infrastr	uctural l	Building	3	••			••		••	11
ICBG Annual	Meetin	g and F	ield Vis	sit				••			12
Key Research	Accom	plishme	ents	••							12
Repor	table ou	tcomes.									12
Conclusion											16
References								••			16
Attachments											17

#### INTRODUCTION:

The African ICBG, in general emphasizes three major goals: evaluation of rainforest plants from Nigeria and Cameroon as cures for parasitic diseases; research on forest dynamics to understand the effects of sustainable harvesting and cultivation of important medicinal plants; training of Cameroonians and Nigerians in natural products chemistry and tropical ecology.

The ICBG project, jointly sponsored by the U.S. National Institutes of Health, the National Science Foundation and the U.S. Department of Agriculture has the main focal point of establishing an integrated program for the discovery of biologically active plants for drug development and biodiversity conservation, while ensuring that source countries derive maximum benefits for their biological resources and their intellectual contribution. BDCP facilitates the drug discovery component of the ICBG and therefore serves as a link between the drug discovery part of the program, the biodiversity conservation component and the economic development projects.

More specifically, the aims of this Associate Program are:

- 1 To conduct ethnobiological inventory of plants in the selected study areas;
- 2. To guide the ICBG in its plant selection and collection strategies for drug discovery. Samples identified from ethnobiological inventory will be collected from biodiversity plots and from wild flora and screened for possible biological activity.
- 3. To perform phytochemistry and preliminary bioassays on selected plants.
- 4. To perform plant extraction, bioassay-guided isolation, structural elucidation with research training and infrastructure development being important components of each operation.
- 5. To maintain and expand the database on African medicinal plants, which includes information on local names, traditional, uses, floristic data, possible constituents, conservation status, agronomic data and economic value. This involved the re-structuring and expansion of the existing AfricMed database to include data from other Associate Programs. This Computerized Information System of African Medicinal Plants (CISAMAP) will be linked to other regional databases.
- 6. To conduct a socio-economic value assessment of the biological resources in the study area which seeks to::
  - I) highlight the non-commercial value of forest products within the cultural/religious context;
  - II) quantify the economic value of biological resources for comparison with other land use options;
  - III) place in priority order the production and marketing of biological resources in local markets to provide income for local residents;
  - IV) provide baseline agronomic data for the formulation of a sustainable management plan for the forest resources; and
  - V) train local natural resource managers and users at the National and Community levels to conduct economic and market research which will integrate the connection between conservation and development. The ICBG may organize rural farmers to cultivate, in fallow areas, certain plants of potential therapeutic value;
- 7. Assist in capacity building of West African scientists in the areas of ethnobiology, inventory and research management. Formal training will be organized in ethnobiological methods and field taxonomy and economic value assessment for local communities.

#### **BODY:**

## 1. Drug Development

The program had continued with extraction and bioassay guided-fractionation of active extracts leading to the isolation of bioactive compounds. The following plants are in our priority list as potential antimalarial candidate. They include; Picralima nitida, Araliopsis tabouensis, Morinda lucida, Enantia chlorantha, Spathodea campanulata, Synclisia scarbrida, Uvaria chamae, Cryptolepis sanguinolenta, Glossocalyx brevipes, Cleistopholis patens, Leidobotrys staudtii and Pachypodanthium staudtii. Three compounds derived from a modification of the parent cryptolepine molecule, which showed very significant antimalarial, have been synthesized to enable in vivo testing. Six compounds identified from earlier studies are being evaluated against four strains of Trypanosoma b. brucei and three T.b. rhodesiense clinical isolates. Four new plants namely Plantex vellous, Glossocalyx brevipes, Fagara lemairei, Dorsternia bateri had showed very promising result (see tables 1, 2) in our trypanosmes and trichomonas test systems. Bioassay-directed fractionation of the above mentioned extracts aimed at isolating the active compounds are in progress. A total of 100 plant extracts were submitted to the University of UTAH for anticancer screen. The above three cryptolepine analogs found to possessing broad spectrum antiprotozoal activity will be screened in vivo against Cryptosporidium and Toxoplasmosis. Results from the non-specific brine-shrimp studies have been analyzed in order to check whether there is any correlation between toxicity to brine shrimp with antimalarial activity. Additional data are being collected to validate this relationship.

## 1.1 Antimalarial activity

A total of 500 samples from plant materials used in traditional medicine for the treatment of different forms of malaria were extracted and submitted to-date for in vitro activity against Plasmodium falciparum, the causative organism for malaria, at the Division of Experimental Therapeutics, Walter Reed Army Institute of Research. The hit rate in this assay for ethnomedically derived samples continues to be very impressive. About 70% showed remarkable activity. Twenty of these have been selected for further studies by bioassay-guided fractionation. Twenty-three antimalarial compounds comprising of twelve different chemotypes have already been isolated and characterized. Two plant families, Annonaceae and Apocynaceae appear to be common ingredients in the preparation of traditional malaria remedies in West and Central Africa. Chemical optimization of cryptolepine analogues is continuing. Sanguinoletine, one of the derivatives of cryptolepine which is 7-fold more potent than chlroquine against the chloroquine-resistant W2 strain of P. falciparum in vitro, has now been synthesized for in vivo animal studies. Results from the non-specific brine-shrimp studies have been analyzed in order to check whether there is any correlation between toxicity to brine-shrimp with antimalarial activity (Table 3).

#### 1.2 Antileishmanial and Antitrypanosomial Activity

Compounds and extracts which showed antileishmanial activity are currently being isolated in large quantities for *in vivo* bioassay. Ten of the extracts tested for *Trypanosoma brucei* consistently gave *in vitro* IC50 values at or below 10ug/ml and were considered sufficiently active to warrant testing of more purified extracts. Three extracts from *Picralima nitida* and two from *Afromomum meleguatta* showed strong *in vitro* activity on four strains of *Trypanosoma b. brucei and three T.B. rhodesiense* clinical isolates. Bioassay guided fractionation of an antitrypanosomal compound with a 10-15-fold increase in the activity of the parent extract. *Glossocalyx brevipes* similarly gave highly active alkaloid compounds with *in vitro* IC50 <1ug/ml.

#### 1.3. Trichomonas

Seven extracts showed activity against Trichomonas. These include three fractions from *Picralima nitida* and two extracts from *Aframomum meleguatta*. These extracts showed remarkable activity two strains of *Trichomonas vaginalis* (both susceptible and resistant strains to metronidazole) and *Trichomonas foetus*. In the trichomonad screen, an extract of *Glossocalyx brevipes* was most active and had an MIC value of 0.0125mg/ml (Table 2).

#### 1.4. Antiviral Activity

Extracts and isolated compounds were screened for activities against HIV, herpes, and yellow fever viruses. Two plant extracts showed high potential activity against HIV. The most active constituent of one extract has been isolated and characterized. One of the plant isolates, which showed in vitro activity against Ebola virus, is being re-tested along with related compounds from *Garcinia kola*.

## 1.5. Opportunistic Infections

Twenty-two extracts were tested against *Cryptosporidium* and *Toxoplasmosis* sp., two samples were found active for each organism. One of the active compounds from *Cryptolepis sanguinolenta*, which showed activity against *Plasmodium falciparum* malaria, was also active against *Toxoplasmosis* and *Cryptosporidium*. Seventeen extracts have also been submitted for testing against Tuberculosis under a NIH program.

## 1.6. CNS Activity

A significant addition to the biological assays is the introduction of the CNS screen at the University of Miami School of Medicine. The first phase of extracts selected by BDCP will be to test low molecular weight \( \beta\)-carboline alkaloids and other atypical anti-psychotics identified through the ethnomedical survey. The compounds will be subjected to the CNS/ receptor transporter screens. Active extracts will be classified according to their ligand binding profiles. High activities and selectivity will indicate active compound profiles at CNS monoamine and opiate systems. These studies will be conducted in receptor-enriched brain or peripheral sources of test screens.

#### 1.7. Cystic Fibrosis

Due to the prevalence of the F508 mutation and the severity of the disease it causes, it is important to understand how the F508 mutation alters channel processing and function as well as to device methods of overcoming these defects. Preliminary studies involve identifying second-site mutations in CTFR F508 that could reverse the F508 processing defect. BDCP and Florida State University are currently developing training curriculum and screens are in the process of being transitioned to our field stations in Nigeria and Cameroon.

## 1.8. Phytomedicine Development

The program research performed under the ICBG has the benefit of providing information that would lead to the development of local herbal medicines, which could then provide a more affordable, and in some cases more effective form of local health care.

The importance of data generated through the pharmaceutical R&D process for the study of traditional medicines for standardization, toxicity and active constituents is often underestimated. A major part of the arrangement under this ICBG is to pass on information concerning acute toxicity of traditional remedies back to the healers so that they can use such remedies more appropriately. In most cases, plants can be formulated directly as phytomedicines based on chemical and biological information obtained from the ICBG preliminary screening results. In view of the ICBG, we have involved the University of Jos, Nigeria who has done a lot of research on phytomedicine in collaboration with associations of healers. The BDCP and the University of Jos currently provides training in standardization of phytomedicines.

## 2. Information Management

Significant efforts have been made in the plan to integrate our existing databases, African Medicinal Plants (AfricMed) and the SI-MAB biodiversity monitoring ecological information (BioMon), and incorporating these with information from economic value assessments and ethnobotanical surveys into a relational database – Computerized Information System on African Medicinal and Aromatic Plants (CISAMAP). CISAMAP is based at the International Center for Ethnomedicine and Drug Development (InterCEDD). The data generated will be made available to federal and state herbaria to promote access to necessary research information in Nigeria and Cameroon. This has an important impact on the improvement of health and resource development in both countries.

#### 3. Socio-Economic Value Assessment Studies

#### 3.1. Overview

The first phase of the economic valuation studies has been completed. This includes house hold studies in two cluster of communities (local government areas) in Imo and Ebonyi States of Nigeria, and Bafut, Sabga and Oku communities of the North West Province of Cameroon. The data from the Cameroonian studies are being analyzed. The report from the Nigerian studies reveals the importance of forest resources to indigenous people. The use of WTP (willingness to pay) estimates when compared to income earned by households from forest products indicates a consumer surplus which reflect the value of natural resources. The efficiency of this measure is however limited by its inability to capture the total value of natural resources. This deficiency will be addressed during the next project phase.

The study also showed strong manifestations of the economic functions of forests which directly or indirectly contributes to the welfare of rural people, especially through the microenterprises it generates. The next phase of the economic valuation studies will therefore focus on the use of microenterprises as a mechanism for internalizing the costs and benefits of biodiversity conservation, and the addition of value to natural resources.

The main objective of the Economic Valuation Studies component of the ICBG was to address the problem of apparent inability of local users and policy makers to recognize or commensurately value the functions and services of tropical forests that has for long constrained conservation efforts. As a result of the improper evaluation of forest resources, the total economic value of forest resources as reflected in official documents and publications rarely influence decisions bordering on their exploitation and management. The underlining aim of the ICBG project was to provide an economic framework for the efficient use and sustainable management of natural resources. Although historically indigenous populations have exploited non-timber forest products (NTFPs) from tropical forests, greater attention has been given to wood and wood products. However, there is now a growing tendency to acknowledge the total value of natural ecosystems, including tropical forests.

The role of economic valuation becomes especially important as a mechanism for capturing and assigning total economic value to natural resources. Through this, it is then possible to show that NTFPs also matter for planning at the microeconomic level, and to demonstrate its necessity in making efficient allocative decisions at the macroeconomic level.

To assess the total value of non-timber forest resources to indigenous communities, survey data was obtained from a sample of households in two local government areas of Imo and Ebonyi states of Nigeria. A total of 300 households living on the fringes of forests and relying on forest resources for most of their consumption goods were sampled.

The survey evaluates the exploitation and uses of various plant species and other forest products in the communities sampled. It assesses the knowledge levels of forest users concerning medicinal plants and other forest products, and determines the use and non-use value of plant species using both the price mechanism and contingent valuation techniques.

## 3.2. Methodology and nature of data

Following a reconnaissance visit to the communities, structured questionnaires were designed to elicit information in these areas:

- 1. Household characteristics
- 2. Products/plants species usually collected from community forests.
- 3. Revenue generated from forest products.
- 4. Gender issues in respect of access to and use of forest products.
- 5. Knowledge of plant species.
- 6. Use and non-use values of plant species.

Data on specific forest products were generated with respect to product type, usual period of collection, quantity and type of product. The revenue generated from harvesting medicinal plants was established by using primary data obtained in the household survey. Specifically, information was sought with respect to the species, plant part collected, period of collection, frequency of collection, quantity, price and market sold.

Finally, contingent valuation methods (CVM) were used to determine willingness to accept compensation from government for loss of a community forest, and willingness to accept compensation for loss of a medicinal plant.

#### 3.3. Results and Discussions

#### Household Profile

The household sample comprised of 248 males and 52 females. Majority of the respondents were in the age bracket of 41-50 years. Most of the survey population had no formal education (76%).

As is typical of occupational distribution patterns in rural areas of Nigeria, 75% of the respondents report farming as their primary occupation, while 36% regarded it as secondary. Other major occupations were traditional herbal practice, wine tapping, civil service and training.

The average household head reported total annual earnings of N22,942 and N15,280 from major and minor occupations, respectively (90 Nigerian Naira = USD1).

## Exploitation and Use of NTFPs

The survey revealed that respondents had free access to community forests, many of which were primary forests, with about 75% of the sample living an average of 3km from a major forest area. The use values structure of forests in the survey show a great diversity of functions to indigenous people in the communities sampled.

Table 4: Major uses of Forests

Uses	No. of Responses	%
Medicinal	158	43.4
Farming and others	144	39.9
Food and other forest products	46	12.6
Culture/Religion	6	1.6
Hunting	4	1.1
Political/Social	4	1.1
Water supply	3	0.8
Total	365	100

Of highest significance to the respondents is the perception that forests provide the habitat for biodiversity, which are considered to have medicinal value. Following closely in importance is farming and other economic activities, which take place in forest areas. Allied to these is the value of forests as a source of food and other forest products such as fruit, nuts, latex, honey, rattan, meat and oils.

The importance of the forest is also reflected in the respondents' ratings of their knowledge levels of plants, especially medicinal plants, high as indicated by about 47% of those surveyed.

Using the price mechanism and direct market values, the study estimated income from food and medicinal plants. Except in a few cases, the data shows a nominal increase in the amount realized from sale of forest products by users. As household incomes become eroded by unfavorable exchange rates, the economic importance of forests and their products relative to agriculture and allied activities begin to rise. This is expected to have negative implications for conservation and sustainable use of biodiversity.

## Non-Market Value of Plant Species

## a. Willingness to Accept Compensation Estimates

An empirical effort is made in this section to measure the value of forest resources, which are not exchanged in the market in other to determine their non-use values. Having first established the preference of the surveyed for such non-marketed plant species, the CVM was employed to determine the willingness to accept (WTA) compensation with respect to medicinal plants.

The WTA estimate per unit of medicinal plant specie was found to range from as low as N20 to as high as N8000. The average estimate of WTA was N2471.92. This was far less than the average for traditional herbalists (N3793.75), which reflects the greater use value from that occupational group. The estimates also reflect a greater value attachment to forest resources with multiple uses.

## b. Willingness to Pay (WTP) Estimate

Respondents were asked how much they were willing to pay as compensation for specific forest areas on the one hand, and specific NTFPs on the other hand. The WTP estimates in respect of specific forests in the communities investigated ranged from N3000 to N6.5million.

The WTP estimates in respect of specific NTFPs were smaller ranging from N100 to N0.5million, with a mean value of N30,278.79, which by implication is the amount an average user of forest products would be willing to pay for its protection.

# c. Willingness to Accept (WTA) Estimate as compensation for Forest Degradation

WTA estimates were also derived from respondents for compensation for forest area degradation and destruction of specific NTFPs, and ranged from N300 to N1.69million. The WTP values for specific forest areas were found to range between N22,000 and N7million, a mean value of N1.5million. The discrepancy in both figures can be attributed to the explanation that people are less willing to spend actual income or wealth as opposed to "opportunity" income or wealth (Knetsch and Sinden, 1984).

#### **Finished Products**

Tropical forests provide essential raw materials and inputs that support assorted rural enterprises and provide employment to large segments of the rural population. Extractives such as oils and wines are common products. Many of the finished products from forest based enterprises have considerable values in both local and international markets, and cover such areas as local crafts

manufacture, processing and artisans.

These enterprises exist in an informal but organized sector, according to nature of activity, producers, processors and marketers. They thus present an unused potential for exploitation in biodiversity conservation.

## 3.4. Implications

The study reveals the importance of forest resources to indigenous people. The use of WTP estimates when compared to income earned by households from forest products indicates a consumer surplus which reflect the value of natural resources. The efficiency of this measure is however limited by its inability to capture the total value of natural resources. This deficiency will be addressed during the next project phase.

The study also showed strong manifestations of the economic functions of forests which directly or indirectly contributes to the welfare of rural people, especially through the microenterprises it generates. The next phase of the economic valuation studies will therefore focus on the use of microenterprises as a mechanism for internalizing the costs and benefits of biodiversity conservation, and the addition of value to natural resources.

## 4. Capacity and Infrastructural Building

The African ICBG has developed a trust fund, benefit-sharing agreements, in-country facilities and training programs to create a sustainable program.

## 1. Capacity building:

We have set up comprehensive phytochemical laboratory services in Nigeria and Cameroon. Our research has shown great promise in the development of new, unique chemicals with therapeutic potential, particularly for malaria and leishmaniasis. These laboratories also provide phytomedicine standardization services to local healers. Good working relationships have been established with local industries so that products developed by the ICBG can be manufactured.

The cornerstone of establishing economic incentives for biodiversity conservation is the provision of a mechanism, which will adequately localize the external benefits it provides and costs associated with using genetic resources. The development of phytomedicines provides such a link. They are relatively low cost to produce and would allow the developing country to keep a greater share of the drug discovery benefit. The return on investment for phytomedicines compares favorably with that from pharmaceutical development. The development of traditional medicinal agents as credible phytomedicines is undoubtedly a more direct way to give value to forest resources.

## 2. Training:

During the 1998-99 year, this ICBG sponsored one participant (Anthony Onugu) to the World Bank Socio-economic training course in Washington DC; two participants to the Convention of Biodiversity Global Forum in Senegal and Costa Rica.

The ICBG has organized and co-sponsored many training courses and workshops on such subjects as: measuring and monitoring biodiversity; plant taxonomy; collection techniques; forest management; cell and tissue culture; enzyme production; DNA manipulation; phytomedicine and pharmaceutical development and the integration of western and traditional medicine. These training programs have brought government experts, academia, and private sector, regulatory authorities, herbalists and pharmaceutical companies together to find practical solutions to

utilizing Africa's immense biodiversity in a sustainable manner. The ICBG is currently supporting two students in phytochemistry, one student in *in vivo* cancer screen studies and one student in Agronomy at M.Sc and Ph.D levels.

### 3. Trust Fund:

A major accomplishment was the establishment in Nigeria of the Fund for Integrated Rural and Development and Traditional Medicine (FIRD-TM). The management of this trust fund is completely independent of the ICBG but administers funds only for the purposes outlined in its charter viz: conservation, drug development and socioeconomic well being of rural communities. The FIRD-TM has an independent board composed of leaders of traditional healers' associations, government officials, representatives of the village council and technical experts from scientific institutions. The predominance of traditional solidarity systems supplies a social structure, which ensures community participation in FIRD-TM projects.

## 5. ICBG Annual Meeting and Field Visit

A team of fifteen delegates visited the BDCP-ICBG project sites in Nigeria and Cameroon during our 1998 annual meeting. The delegation included the ICBG principal investigator, Associate program leaders and representatives of the funding agencies. The team while I Nigeria visited Federal Environmental Protection Agency (FEPA) at Abuja, National Agency for Food and Drug Control (FDA), University of Jos and International Centre for Ethnomedicine and Drug Development (InterCEDD). The annual meeting was held at the BDCP Conference hall in Nsukka, Nigeria on October 31, 1998. The team also visited other ICBG sites such as University of Dchang, ICBG 50-hectare plot at Korup, Cameroon.

#### **KEY RESEARCH ACCOMPLISHMENTS:**

(Bulleted list of key research accomplishments emanating from this research.)

#### **REPORTABLE OUTCOMES:**

#### **Books**

1. Maurice M. Iwu, Elijah N. Sokomba, Chris O. Okunji, Chioma Obijiofor and Iwe P. Akubue: Commercial Production of Indigenous Plants As Phytomedicines and Cosmetics; BDCP Press (1997)

### Chapters in Books

- 1. Iwu, Maurice & Sarah Laird Health, Conservation, and Economic Development: The International Cooperative Biodiversity Group Drug Development and Biodiversity Conservation in Africa A Benefit Sharing Plan", In: Rainforest Alliance's Natural Resources and Rights Program. edited by Charles Zerner, 1997.
- 2. Iwu, Maurice Resource Utilization and Conservation of Biodiversity in Africa", Medicinal Resources of the Tropical Forest: Biodiversity and its Importance to Human Health edited by Micheal Ballick, Elaine Elisabetsky and Sarah Laird.
- 3. Iwu, M.M., Inya-Agha, S.I., Anderson, S.L., and Schuster, B.G. <u>In vitro</u> Antimalarial Activity of Indole Alkaloids From Picralima Nitida Fruits" *Planta Medica*, in press.

#### **Peer Reviewed Articles**

- 1. Awachie, P.I.A. and Ugwu, F.O., Preliminary Investigation of the Antimicrobial and Brine Shrimp Lethality Properties of Nigerian Medicinal Plants", *Int. J. of Pharmacognosy*, vol. 35 (5), pp. 338-343, 1997.
- 2. Ayafor J.F., Ngnokam, D., Tsopmo, A., Okunji, C.O. 1998. Antimalarial activity of Urea Derivatives from *Pentadiplandra brazzeana*. Ethnopharmacology (In Review).
- 3. Tsopmo, A., Tene, M. Kamnaing, P., Ayafor J.F., and Sterner, O. (1998.) C-geranylated flavonoids from *Dorstenia poinsettifolia* Phytochemistry (In Press).
- 4. Schuster, BG., Jackson, JE., Obijiofor, CN., Okunji, CO., Milhous, W., Loso, E., Ayafor, JF and Iwu, MM (1999) Drug Discovery and Conservation of Biodiversity in West and Central Africa: a new standard of collaboration with indigenous people, *Journal of Pharmaceutical Biology* (in press).

## Presentations at Meetings, Conferences

- 1. Akubue, P.I., Onyechere, C., Obijiofor, C., Duncan, A.R., Okunji, C.O., Azuine, M.A., Iwu, M.M., Clinical Evaluation of Kola in Human Volunteers, apaper delivered at the American Society of Pharmacognosy Interim Meeting, April 29-May 1, 1999 Grand Casino convention Center and veranda Hotel Tunica, Mississippi.
- Ayafor J.F., Sterner, O., Tene, M. and Iwu M.I. 1997. Flavonoids and other constituents of Cameroonian *Dorstenia* species. 7<sup>th</sup> NAPRECA Symposium on Natural Products. Dar Es Salaam, Tanzania, August 17-22, 1998.
- 3. Iwu Maurice M, Angela R. Duncan, Chris O. Okunji, New Antimicrobials of Plant origin New Crops and New Uses, Prospective in New Crops and New uses pp 447-452, 1999
- 4. Iwu M. Maurice, Biodiversity Utilization and Conservation in West and Central Africa; being a plenary lecture delivered at the 2nd IUPACInternational Conference on Biodiversity, 11-15th July 1999, Belo Horizonte, MG, Brazil.
- 5. Iwu M. Maurice, Okunji O. Chris, Ayafor F. Johnson, Akubue, P.I, Jackson E.Joan, Tally D. John, Cyrus Bacchi and Schuster B.G.; Antiprotozoal AgentsFrom African Medicinal Plants Based on Ethnomedical Leads; being an invited paper delivered at the 2nd IUPAC International Conference on Biodiversity, 11-15th July 1999, Belo Horizonte, MG, Brazil
- 6. Iwu Maurice M, Angela R. Duncan, Chris O. Okunji New Antimicrobials of Plant Origin New Crop and New uses: Biodiversity and Agricultural Substainability. Association for the advancement of Industrial Crops Purdue University Center for New Crops & Plant Products New Uses Council, Inc. November 8-11, 1998, Hyatt Regency Hotel, Phoenix, Arizona.

- 7. Iwu, MM; Schuster, BG and Obijiofor, CN "ICBG: A new Level of Collaboration with Indigenous People"; International Society of Ethnobiology Congress, Whakatane, New Zealand (Nov. 1998)
- 8. Nnadozie K., Access and Benefit sharing: Trust Fund Experience in Nigeria. A paper presented at the Regional TRIPS Review Conference, Nairobi Kenya, April 1999.
- 9. Okunji O Chris. Skanchy J. David, and Iwu M. Maurice, QuantitativeEstimation Of Kolaviron In *Garcinia Kola* Preparations Using CapillaryElectrophoresis, paper delivered at the American Society of Pharmacognosy Interim Meeting, April 29-May 1, 1999 Grand Casino convention Center andveranda Hotel Tunica, Mississippi.
- 10. Onugu Anthony, New energy and development options for West Africa under the Clean Development Mechanism, presented at the Indigenous People's workshop Global Biodiversity Forum, June 1999, Costa Rica.
- 11. Onugu Anthony, Capturing the total value of natural resources, paper delivered at the Global Biodiversity Forum, December 1998, Dakar Senegal.

## **Conference Proceedings**

- 1. Iwu, MM. Bioprospecting and Concerns of Indigenous People. In: Delores A. Wozniak, Sylvia Yuen, Mario Garrett, Tarek Shuman (eds)(1997) International Symposium on Herbal Medicine A Holistic Approach. Proceedings of a conference, 1-4 June 1997, Honolulu, Hawaii. pp. 393-424
- 2. Iwu, MM Production of Phytomedicines and Cosmetics from Indigenous Genetic resources: from Lab to market., In: Maurice Iwu, Elijah Sokomba, Chris Okunji, Chioma Obijiofor and Iwe Akubue (Eds). (1997) Commercial Production of Indigenous Plants as Phytomedicines and Cosmetics, pp. 1-19.
- 3. Iwu, M.M., Bioprospecting Using African Genetic Resources", In: K.E. Hoagland and A.Y. Rossman (eds). Global Genetic Resources: Access, Ownership and Intellectual Property Rights Association.
- 4. Okunji, CO., Jackson, JE., Tally, JD., Iwu, MM and Schuster, BG. Bioassay Approach to Medicinal Plant Research. In: Maurice Iwu, Elijah Sokomba, Chris Okunji, Chioma Obijiofor and Iwe Akubue (Eds). (1997) Commercial Production of Indigenous Plants as Phytomedicines and Cosmetics. pp. 121-133.

#### **Non-peer-reviewed Articles**

1. Dallmiere F., Sunderland T., Ros C. and Njamadje A. Biodiversity Research and Monitoring Training Manual, Cameroon, 1997.

- 2. Obijiofor, C.N. Iwu, M.M. and Schuster B.G. "International Cooperative Biodiversity Group (ICBG) on Drug Development and Conservation of Biodiversity in West and Central Africa" presented at the BDCP/ICS-UNIDO International Workshop, Enugu, Nigeria (1997)
- 3. Obijiofor, C.N. "Integration of African Ethnomedicine and Western healthcare system" presented at the Organization Theory: Strategy and Structure symposium, CMU-WRAMC (1998)

#### **Patents Disclosures**

- 1. Antiparasitic and antifungal compositions, mechanism of action, andmethods of use Inventors: Joan E. Jackson, Maurice M. Iwu, Chris O. Okunji, Cyrus Bacchi, John D. Tally, and Johnson F. Ayafor, U.S Dislosure 1998
- 2. Plant-derived antiparasitic and antifungal compounds, mechanism ofaction, and methods of use Inventors: Chris O. Okunji, Maurice M. Iwu, JoanE. Jackson, John D. Tally, and Cyrus Bacchi and Johnson F. Ayafor U.S Dislosure 1998

## Degrees obtained that are supported by this award:

- 1. Appollinaire Tsopmo M.Sc from University of Dschang, Cameroon
- 2. Franca Ugwu Ph.D from Catholic University, Berlin.

#### Informatics such as databases and animal models:

- 1. AfricMed: An inventory of plants used in traditional medicine in West and Central Africa and epidemiological surveys of the use of these plants.
- 2. ICBG-WRAIR Drug Development Inventory: A database of plant material, extractions, chemistry and biology.
- 3. Biodiversity Measuring and Monitoring (BioMon) database: A database of plants found in the network of ICBG small biodiversity plots in Nigeria and cameroon. It has the capability to plot sample collection locations on maps as well as digital overlays of roads, rivers, railways and topography of West and Central Africa.
- 4. Korup Dynamic Project (KDP) Tree Demographic database: A database of plants found in the ICBG 50-hectare biodiversity plot on the Nigeria-Cameroon border line. Both BioMon and KDP are linked to the Smithsonian network of similar plots all over the world.
- 5. Computerized Information System on African Medicinal and Aromatic Plants (CISAMAP): All ICBG databases are being integrated into this database. Efforts are also being made to integrate this in an on-line format.

#### Funding applied for based on work supported by this award

None

#### **CONCLUSIONS:**

BDCP made significant progress in all aspects of its scope of work and has created a sustainable program, which will last beyond the life of the ICBG. BDCP will continue its plant collection, phytochemistry, drug development and capacity building efforts.

#### REFERENCES:

- Abe I, Tomesch JC, Wattanasin S, Prestwich GD, 1994. Inhibitors of squalene biosynthesis and metabolism. Natural Products Reports 11:279-302.
- Desjeux P and UNAIDS, 1998. Leishmania and HIV in Gridlock. World Health Organization/UNAIDS, Geneva, Switzerland, 28 pp..
- Dickson JK Jr, Biller SA, Magnin DR, Petrillo EW Jr, Hillyer JW, Hsieh DC, Lan S-L, Rinhart JK, Gregg RE, Harrity TW, Julibois KG, Kalinowski SS, Kunselman LK, Mookhtiar KA, Ciosek CP Jr, 1996. Orally active squalene synthetase inhibitors: bis((acyloxyl)alkyl) prodrugs of the alpha-phosphonosulfonic acid moiety. J Med Chem 39:661-664.
- Draper D, et al., 1998. Trichomoniasis opens the door for HIV infection. J Infect Dis 178(3):815-819.
- Endo A, Hasumi K, 1993. HMG-CoA reductase inhibitors. Natural Products Reports 10(6):541.
- GarberK, 1999. How Lipitor stole Zocor's lunch. Modern Drug Discovery Mar/Apr1999:17-18.
- Gould AL, Furberg CD, Heyse JF, Santanello NC, Rossouw JE,1995. Cholesterol reduction yields clinical benefit. A new look at old data. Circulation 91(8):2274-2282.
- Lipper RA, 1999. E pluribus product. Modern Drug Discovery Jan/Feb99:55-60.

Steck EA, 1972. The Chemotherapy of Protozoan Diseases, Vol II, pp. 7.61-7.63, & 11.100-110, US Government Printing

#### **APPENDICES:**

- Table 1: In vitro Activity of Plant Extract Against Growth of African Trypanosomes
- Table 2: Minimum Inhibitory Concentration (MIC) of Plant Extracts against *Trichomonas* vaginalis strain CI-NIH
- Table 3: In vitro Antimalarial Activity of Plant Extracts Against Two Clones of Plasmodium falciparum and Brine shrimp.
- Table 4: Major Uses of Forests

In vitro Activity of Plant Extract Against Growth of African trypanosomes.

Table 1

		<u>IC<sub>50</sub> (μg/ml)</u>		
	EATRO 1 10	KETRI 243	KETRI 269	KETRI 243- As-10 3
Di analima niti da mfr)	9.2	15.1	8.4	8.5
Picralima nitida pfr2	1.1	6.1	8.2	11
Picralima nitida pfr3	64	5	500?g/ml-22%	5OO?g/ml-13%
Picralima nitida pfr4	102	21.5	5OO?g/ml-22%	47
Aframomum melegueta hex	9.0	8.5	12.6	14.9
Aframomum melegueta CHCl <sub>3</sub>	8.4	7.2	15	30
Aframomum melegueta MeOH	500?g/ml-38%	500?g/ml-14%	5OO?g/ml-44%	5OO?g/ml-22%
Aframomum melegueta aq	134	74	79	51
Gongronema latifolium CHCl <sub>3</sub>	500?g/ml-16%		500?g/ml-7%	500?g/ml8%
Gongronema latifolium ext		2.0	1.6	3.4
Grape seed2032	1.9	19.6	28.9	40.55
Albizia ferruginea hex	18.0		114	117
Uvaria chamae rt DCM	115	229	30.0	39.0
Morinda lucida DCM	33	32.5		6.2
Dracaena mannii pDM-X	6.5	5.4	6.8	13.5
Picralima nitida PNP-2	15.0	16.9	18.0	12.6
Picralima nitida PNP-4	13.5	8.3	12.5	15.1
Picralima nitida PNP-8	14.1	16.0	18.0	78
Kigelia africana MeOH	119	73.0	74	
Araliopsis tabouensis MeOH	6.4	64.0	59	105
Mezoneurum benthamianum CH <sub>2</sub> Cl <sub>2</sub>	44	19.5	18.5	-
M. benthamianum MeOH	19	<b>7</b> 6	37	-
Eupatorium odoratum comp (Sakuranetin)	20	20.5	73	-
Gnetum africanum CHCl <sub>3</sub>	202	190	225	-
Plantex vellous CH <sub>2</sub> Cl <sub>2</sub>	75	18.5	13.5	-
Plantex vellous MeOH	1.5	-	13	-
Fagara lemairei MeOH	2.2	2	2.05	_
Fagara lemairei CH <sub>2</sub> Cl <sub>2</sub>	20.5	170	130	-
Erythrina senegalensis CH <sub>2</sub> Cl <sub>2</sub>	7.2	9.1	15.5	-
Erythrina senegalensis MeOH	18.9	20	22	-
Mitracarpus scaber	98	105	71	-
Olax viride	195	32%@ 500μM	235	-
Chasmanthera dependens.	225	225	-	-
Dracaena mannii Spiroconazole	200	200	200	-
Glossocalyx brevipes Neutral fraction	0.78	0.76	0.715	-
Dorsternia barteriDB2	7.5	7.3	15.25	-
Dorsternia barteri CH <sub>2</sub> Cl <sub>2</sub>	16.5	19.5	16	-
Gnetum africanum MeOH	54	60	•	-
Eupatorium odoratum Fr. 60	50	47	-	-
Garcinia kola Heckel	210	210	-	-
Pentamidine	0.00048	0.00186	0.00192	0.003
Melarsen Oxide	0.00077	0.0025	0.0066	0.0072
IATOMIDON OUM				

Table 2

Minimum Inhibitory concentration (MIC) of Plant Extracts against Trichomonas vaginalis strain CI-NIH

	MIC (mg/ml)					
		CI-NIH	CDC-085	KV-1		
	Lab. No	48 hrs	48 hrs	48 hrs		
Gongronema latifolium	SU-105	>2.50	2.50	2.50		
Dracaena mannii	SU-175	2.50	2.50	2.50		
Picralima nitida	SU-367	12.50	12.50	0.78		
Picralima nitida	SU-369	0.62	1.25	1.25		
Picralima nitida	SU-370	2.50	2.50	2.50		
Gongronema latifolium CHCl3	SU-614	1.25	0.62	1.25		
Albizia ferruginea hex	SU-679	0.62	0.62	0.62		
Grape fruit seed 2032	SU-719	0.31	0.01	0.15		
Araliopsis tabouensis MeOH fr	SU-724	0.62	0.62	2.50		
Morinda lucida DCM	SU -740	1.25	1.25	1.25		
Aframomum melegueta hex	SU-766	1.25	1.25	2.50		
Kigelia africana MeOH	SU-769	0.31	0.62	0.62		
Aframomum melegueta CHC13	SU-787	0.62	1.25	2.50		
Aframomum melegueta MeOH	SU-798	1.25	0.62	.25		
Uvaria chamae rt DCM	SU-799	0.15	0.31	0.62		
Aframomum melegueta aqueou	ısSU-813	2.50	2.50	0.15		
Picralima nitida PNP-2	SU-846	2.50	1.25	2.50		
Picralima nitida PNP-4	SU-847	2.50	2.50	2.50		
Picralima nitida PNP-8	SU-848	2.50	2.50	2.50		
Metronidazole		0.003	0.40	0.004		

Table 3

# In vitro Antimalarial Activity of Plant Extracts Against Two Clones of Plasmodium falciparum and Brine shrimp

	IC <sub>50</sub> µg/ml					
Plants	Parts/extracts	D-6	W-2	LD <sub>50</sub> / 95%CL		
Cleistopholis patens .	CLPS- MLsMeOH	7102	14556	3.36*		
Mezoneurum benthamianum	MEBM- LMLsMeOH	50000	50000	84.8		
Mezoneurum benthamianum	MEBNLMDMLs (1:1)	33465	22537	5314		
Mezoneurum benthamianum	MEBN- LsH2O LMH2O	NT	NT	3014		
Pachypodanthium staudtii	PASI-M BkMeOH	270	474	43.8		
Pachypodanthium staudtii	PASI- DMBkCH2Cl2	126	138	30.7		
Picralima nitida	PINAR-Fr- Fr33Rind	337	745	284.02		
Dracaena mannii	DAMI- FPMMRFp221Fr	NT	NT	67.7		
Enantia chlorantha	ENCA- DMBkCH2Cl2	504	1070	0.78		
Enantia chlorantha	ENCA- MBkMeOH	133	121	71.64*		
Lepidobotrys staudtii	LEPIDO- DMLLs CH2Cl2	4389	4507	0.75**		
Lepidobotrys staudtii	LEPIDO- LMLsMeOH	2533	2082	8.30**		
Pyrenacantha staudtii Engl.	LfMeOH	25861	>50000	774.05		
Gongronema latifolium	lf/st	30590	13506	11.26		

· NB

\* = at 100mg

\*\* = at 10mg

NT = not tested